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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,407	06/02/2005	Shigehiko Imagawa	273056US0PCT	4976

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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
O'DELL, DAVID K	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
09/02/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/537,407	IMAGAWA ET AL.	
	Examiner	Art Unit	
	David K. O'Dell	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *16-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/2/2005, 8/31/2005, 7/5/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

2. Claims 1-45 are pending. Claims 16-45 are withdrawn from consideration.

Response to Restriction Election

3. Applicant's election without traverse of Group I and the species "4-[N-(4-methoxyphenyl)-N-[[5-(3,4,5-trimethoxyphenyl)pyridin-3-yl]methyl]amino]- 1-[[2-(3,4,5-trimethoxyphenyl)pyridine-4-yl]methyl]piperidine or a salt thereof or a solvate thereof" (Example 13, on page 52, not the Example on page 29) in the reply filed on January 9, 2008 is acknowledged. The election was made without traverse, and the species election is in error since a single disclosed species does not include solvates. Nonetheless, the examiner had examined the solvates along with the compound. This application contains claims drawn to a nonelected invention with traverse. A complete reply to this action must include a cancellation of nonelected claims or other appropriate action.

Group I, claims 1-15, drawn to compounds and compositions with a pyridyl-piperidinyl-pyridyl core where in formula 1 claim 1, l is 1; m is 0, X is NR_4, R_4 is phenyl, W1 = W2 = N, shown as structure **I** figure 1, If this group is elected, a further election of a single disclosed species is also required.

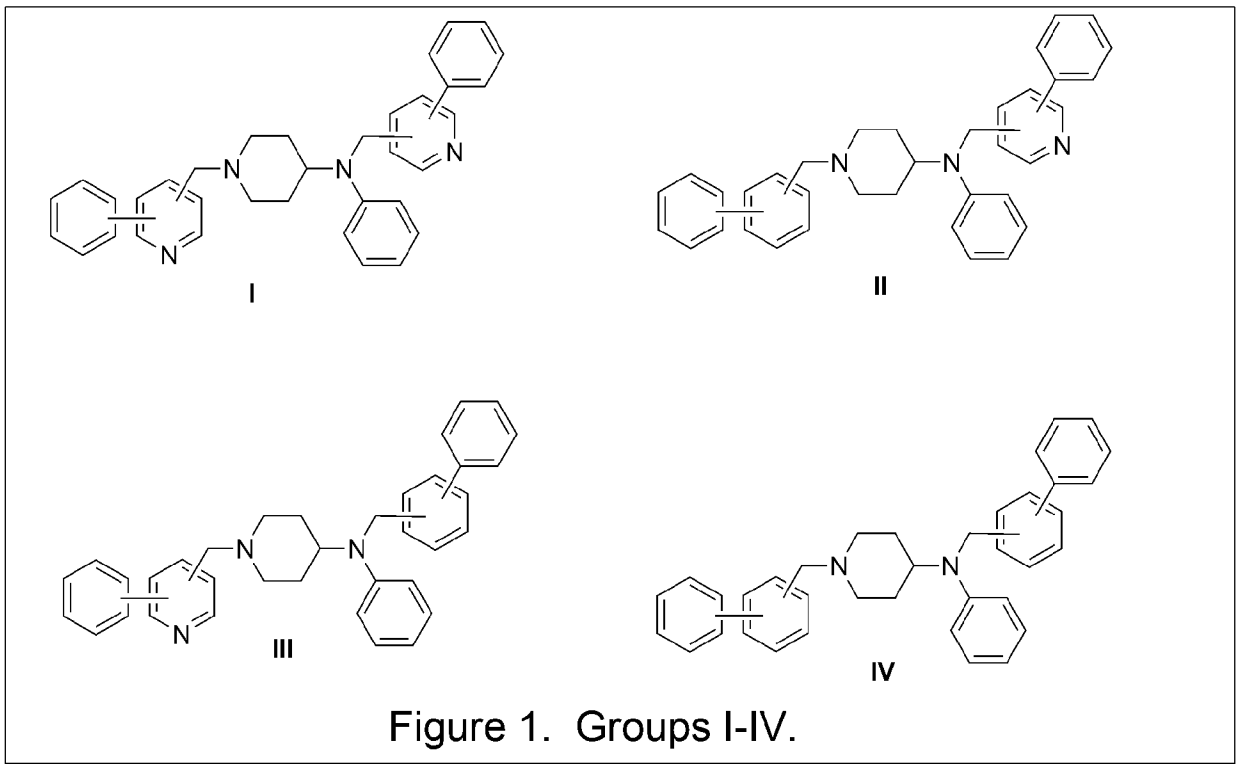
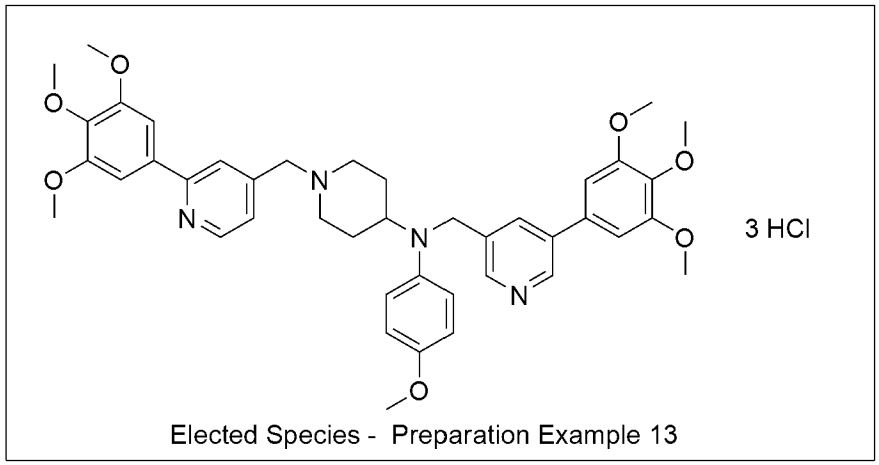


Figure 1. Groups I-IV.



Elected Species - Preparation Example 13

Priority

3. This application is a national stage of PCT/JP03/15589 filed 12/05/2003 which claims benefit of U.S. Provisional Application: 60/431,234 file 12/06/2002. The U.S. provisional application is filed in a language other than English. An English translation of the non-English language provisional application and a statement that the translation is accurate must be filed in

provisional application No. 60/431,234. See 37 CFR 1.78(a)(5). The English translation and a statement that the translation is accurate required by 37 CFR 1.78(a)(5) is missing. Accordingly, applicant must supply 1) the missing English translation and a statement that the translation is accurate in provisional application No. 60/431,234 and 2) in the present application, a confirmation that the translation and statement were filed in the provisional application. If 1) and 2) are not filed (or the benefit claim withdrawn by the filing of an amendment or Supplemental Application Data Sheet) prior to the expiration of the time period set in this Office action, the present application will be abandoned. See 37 CFR 1.78(a)(5)(iv).

Claim Objections

4. Claim 15 is objected to for the following informality. Pyridine has been misspelled as "piridine", appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim and are drawn to compounds and compositions with the recitation of functional language "a preventative or therapeutic agent for pathological conditions caused by reduced production of erythropoietin". Based on the election following the restriction requirement these appear to be compound claims not method claims. If these are in fact compound claims, the functional language should be removed. See *Union Oil Co. of California v. Atlantic Richfield Co.* 54 USPQ2d 1227 where "composition claims cannot, as the appellant

refiners argue, embrace only certain uses of that composition. (citing *In Re Spada*) Otherwise these composition claims would mutate into method claims." If the applicant has intended to claim a method of treatment, the wrong group was chosen, however **a** method of treating commensurate in scope with the allowed compound claims may be rejoined if the compounds become allowable. The claims will be examined to the extent they cover compounds and compositions, not as they relate to any method of treating, etc.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-15 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. 6,395,753. The elected species is listed as Example 13 in column 49.

6. Claims 1-15 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. 6,498,169. The elected species is listed as Example 13.

7. Claims 1-15 are rejected under 35 U.S.C. 102(a) as being anticipated by U.S. 6,605,620. The elected species is listed as Example 13.

8. Claims 1-15 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. 6,867,221. The elected species is listed as Example 13.

The applied reference has a common assignee, and some inventors in common with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

9. Claims 1-15 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. PG Pub 20050176764. The elected species is listed as Example 13.

The applied reference has a common assignee, and some inventors in common with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim Rejections - 35 USC § 112 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to

"preventative or therapeutic agent for pathological conditions caused by reduced production of erythropoietin", which apparently includes various anemia, "chronic anemia, renal anemia, aplastic anemia, or pure red cell aplasia". claims 6 & 11, however no compound has ever been found to treat or prevent all conditions caused by reduced production of erythropoietin. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "silver bullet" is contrary to our present understanding of these various disorders. "Fanconi anemia (FA) is an autosomal-recessive leukemia susceptibility syndrome characterized by multiple congenital anomalies and childhood-onset aplastic anemia." Toshiyasu Taniguchi "Molecular Pathogenesis of Fanconi Anemia" *International Journal of Hematology*, **2002**, *75*, 123-129. Thus it is clear that genetic disorders such as Fanconi anemia cannot be prevented unless one is suggesting that the compounds of the instant claims manipulate a patients DNA prior to the formation of the patient. Red cell aplasia is not even understood and certainly cannot be prevented. "The pathogenesis of the disease is not yet clarified…….Since the etiology of the disease is unclear, a definite treatment is not available." M. Djaldetti "Pure red cell aplasia—a rare disease with multiple causes." *Biomedicine & Pharmacotherapy* **2003**, *57*, 326–332. Thus, it is beyond the skill of medical doctor today to get an agent to be effective against all anemia. In fact anemia is not pathological condition, but rather the result of a blood test. Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the use of the instant compounds. Moreover the specification does not seem to disclose exactly what "pathological conditions" actually are, much less any data indicating that any of the disclosed compounds are involved in the treatment of "pathological conditions".

11. Claims 27 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making solvates of the claimed compounds. The specification does not enable any person skilled in the art of synthetic organic chemistry to make the invention commensurate in scope with these claims. "The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. In the present case the important factors leading to a conclusion of undue experimentation are the absence of any working example of a formed solvate, the lack of predictability in the art, and the broad scope of the claims. g) The state of the art is that is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). West, Anthony R., "Solid State Chemistry and its Applications, Wiley, New York, 1988, pages 358 & 365. The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is their compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometery of the formed solvate, i.e. if one, two,

or a half a molecule of solvent added per molecule of host. In the same paragraph on page 365 West (Solid State Chemistry) explains that it is possible to make meta-stable non-equilibrium solvates, further clouding what Applicants mean by the word solvate. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stabile region of the solvate. h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula I as well as the presently unknown list of solvents embraced by the term "solvate". Thus, the scope is broad.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,395,753. Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims although somewhat narrower are overlapping in scope with those of the '753 patent, and cover the same compounds.

13. Claims 1-15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of 1-14 U.S. Patent No. 6,498,169. Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims although somewhat narrower are overlapping in scope with those of the '169 patent, and cover the same compounds and compositions.

14. Claims 1-15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 4, 5 of U.S. Patent No. 6,605,620. Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims cover genera, species, and compositions that are those species of the '620 patent.

15. Claims 1-15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,867,221. Although the conflicting claims are not identical, they are not patentably distinct from each other because the

current claims although somewhat narrower are overlapping in scope with those of the '221 patent, and cover the same compounds.

Conclusion

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David K. O'Dell whose telephone number is (571)272-9071. The examiner can normally be reached on Mon-Fri 7:30 A.M.-5:00 P.M EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0684. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D.K.O.

/Rita J. Desai/
Primary Examiner, Art Unit 1625